REMARKS

This Response, filed in reply to the Office Action dated May 7, 2008, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1, 2, 4-7 and 17 are all the pending claims and are rejected. Entry and consideration of this response are respectfully requested.

Claim Rejections Under 35 U.S.C. § 101

At page 3 of the Office Action, claims 1, 2, 4-7 and 17 are rejected under 35 U.S.C. § 101 because claimed invention is allegedly not supported by either a specific and substantial credible asserted utility or a well established utility. Specifically, the Examiner asserts that the specification does not disclose biological role of C1 protein of SEQ ID NO: 1 and its relevant to any specific physiological process or clinical condition.

Applicants respectfully disagree.

The biological activity of C1 protein of SEQ ID NO: 1 is taught in the Examples of the present application. Specifically, the Examples teach i) that expression of C1 is enhanced in rat primary nerve cells that have been subjected to endoplasmic reticulum stress (Example 1), ii) that the expression of C1 is also enhanced in rat primary nerve cells that have been stimulated with J3 amyloid (Example 2), iii) that C1 promotes cell death in SK-N-AS cells (human neuroblastoma) (Example 4), and iv) that C1 inhibits secretion of Aβ40 and Aβ42 in IMR-32 cells (human neuroblastoma) (Example 5). Moreover, as the Examiner established, "Example 4, p.69 of the instant specification demonstrates that cells transfected with C1 gene had increased survival rate as compared to control cells (see Figure 1 and 2)." Page 4, *Office Action of May 7,*

2008. The instant specification indeed discloses the biological roles of the C1 gene and, thus, its encoding protein.

Moreover, regarding the C1 protein's relevance to neurodegenration, without agreeing to the Examiner's argument, Applicants limit the utility of the claimed production to Alzheimer's disease, instead of neurodegenerative diseases.

As clearly indicated in Example 5 of the present specification, Aβ40 concentration (Fig. 3) and Aβ42 concentration (Fig. 4) were reduced in the culture supernatant of the cells transformed with C1, as compared with the IMR-32 cells transformed with GFP (control cells). In other words, Example 5 shows that C1 inhibits secretion of Aβ40 and Aβ42 in human neuroblastoma cells. Furthermore, the Examiner also admits at least the C1 protein's relevance to β-amyloid peptide (Aβ) by stating, "Example 5, p. 69 of the instant specification describes results of experiments, in which cells transformed with C1 gene were recorded to secrete less Aβ than control cells." Page 4, *Office Action of May 7, 2008.*

However, the Examiner states, "there is no explanation given as how spontaneous secretion of Aβ in cells transfected with C1 relates to etiology of Alzheimer's disease in particular … ." Pages 5-6 of *Office Action of May 7, 2008.* In response, Applicants assert that the state of art at the time of invention has established such connection between Alzheimer's disease and Aβ. For example, in Seubert et al. (NATURE Vol. 359, 325-327, Sep. 1992), soluble Alzheimer's Aβ was isolated and quantified from in human biological fluids, and Seubert clearly stated that "(t)hese observations offer new opportunities for developing diagnostic tests for Alzheimer's disease and therapeutic strategies aimed at reducing the cerebral deposition of Aβ." *See* Page 325, right column, first paragraph.

Additionally, the Examiner asserts, "[c]haracterization of the claimed nucleic acids of SEQ ID NO: 2 and encoded protein of SEQ ID NO: 1 as affecting secretion of Aβ or survival of cells artificially transfected with the protein is clearly not sufficient to establish their utility." However, as pointed out above, Applicants submit that such inhibition effect of the claimed invention on the secretion of Aβ proves the specific, substantial and credible utility to diagnose and treat Alzheimer's disease. Indeed, Siemers et al. (Clin Neuropharmacol 2007, 30: 317-325; Clin Neurophainiacol 2005, 28: 126-132), and Fleisher et al. (Arch Neurol 65(8), 1031-1038, 2008) report clinical trails for the compound LY450139 having the Aβ secretion inhibitory activity to evaluate its safety, tolerability and Aβ response as a therapeutic agent for Alzheimer's disease. *See* Pages 318-319 of Siemers et al. and page 127 of Fleisher et al.

For the reasons set forth above, the present specification teaches the biological roles, such as the apoptosis promoting activities, of the C1 protein. Moreover, in view of the established technical knowledge possessed by one of ordinary skill in the art as of the priority date of the present application, one in the art would also have recognized that the C1 gene and its encoding protein can be used in diagnostic and therapeutic strategies aimed at reducing the cerebral deposition of Aβ and, thus, at treating Alzheimer's disease. Therefore, one in the art would have further recognized that the claimed invention has specific, substantial, and credible utility for screening compounds that inhibit the apoptosis promoting activities of such C1.

Withdrawal of the rejection is therefore kindly requested.

Claim Rejections Under 35 U.S.C. § 112, first paragraph

At page 8 of the Office Action, the Examiner rejects Claims 1, 2, 4-7 and 17 under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner alleges that, since the claimed invention is not supported by either a specific and substantial credible asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention.

Applicants respectfully assert that the C1 protein and nucleic acids to encode the C1 protein are supported by a specific, substantial, and credible utility for the identical reasoning listed above. Namely, the claimed invention can be used for diagnosing and treating Alzheimer's disease, and one of ordinary skill in the art would recognize how to use the claimed invention.

Therefore, Applicant respectfully requests reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 112, second paragraphs

At page 8 of the Office Action, the Examiner rejects Claim 17 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner asserts that claim 17 is indefinite as being incomplete for omitting essential elements that comprise the instant claimed kit. The Examiner asserts, "[s]ince the activity of the protein of SEQ ID NO: 1 is not known ... and because there appears to be no patentably significant utility in screening for compounds that affect the activity of the protein of SEQ ID NO: 1, one skilled in

the art would not know as what material limitations define the claimed subject matter, a kit comprising protein of SEQ ID NO: 1.

Applicants respectfully disagree. The specification provides ample support for the activity of the C1 protein for the reasons set forth above. Specifically, C1 promotes cell death in SK-N-AS cells (human neuroblastoma) (Example 4) and inhibits secretion of Aβ40 and Aβ42 in IMR-32 cells (human neuroblastoma) (Example 5). Moreover, as the Examiner established, "Example 4, p.69 of the instant specification demonstrates that cells transfected with C1 gene had increased survival rate as compared to control cells (see Figure 1 and 2)." Page 4, *Office Action of May 7, 2008.* As the present Examples disclose the activities of the C1 protein, and one of the ordinary skill in the art would recognize the utility of such protein in diagnosing and treating Alzheimer's disease as discussed above, one in the art would also recognized what is distinctly claimed by "a kit for screening a compound or its salt that promotes or inhibits the activity of the protein or its salt" as claimed.

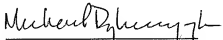
Therefore, Applicant respectfully requests reconsideration and withdrawal of this rejection.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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